

#23



ENTERED

1600

## RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/471,669A

DATE: 12/23/2002 P-6

TIME: 12:15:54

Input Set : A:\Sub15270-006430US.app

Output Set: N:\CRF4\12232002\I471669A.raw

```
3 <110> APPLICANT: Anderson, John P.
4      Basi, Guribbal
5      Doane, Minh Tam
6      Frigon, Normand
7      John, Varghese
8      Power, Michael
9      Sinha, Sukanto
10     Tatsuno, Gwen
11     Tung, Jay
12     Wang, Shuwen
13     McConlogue, Lisa
14     Elan Pharmaceuticals, Inc.
16 <120> TITLE OF INVENTION: BETA-SECRETASE ENZYME COMPOSITIONS AND METHODS
18 <130> FILE REFERENCE: 015270-006430US
20 <140> CURRENT APPLICATION NUMBER: US 09/471,669A
21 <141> CURRENT FILING DATE: 1999-12-24
23 <150> PRIOR APPLICATION NUMBER: US 60/114,408
24 <151> PRIOR FILING DATE: 1998-12-31
26 <150> PRIOR APPLICATION NUMBER: US 60/119,571
27 <151> PRIOR FILING DATE: 1999-02-10
29 <150> PRIOR APPLICATION NUMBER: US 60/139,172
30 <151> PRIOR FILING DATE: 1999-06-15
32 <160> NUMBER OF SEQ ID NOS: 108
34 <170> SOFTWARE: PatentIn Ver. 2.1
36 <210> SEQ ID NO: 1
37 <211> LENGTH: 1503
38 <212> TYPE: DNA
39 <213> ORGANISM: Homo sapiens
41 <400> SEQUENCE: 1
42 atggcccaag cctgcccctg gtcctgctg tggatgggcg cgggagtgct gcctgcccac 60
43 ggcacccagc acggcatccg gctgcccctg cgcagcggcc tggggggcgc ccccctgggg 120
44 ctgcggtctg cccgggagac cgacgaagag cccgaggagc ccggccggag gggcagcttt 180
45 gtggagatgg tggacaacct gaggggcaag tccggggcagg gctactacgt ggagatgacc 240
46 gtgggcagcc ccccgagac gctcaacatc ctggtggata caggcagcag taactttgca 300
47 gtgggtgctg ccccccaccc cttcctgcat cgctactacc agaggcagct gtccagcaca 360
48 taccgggacc tccggaaggg tgtgtatgtg ccctacaccc agggcaagtg ggaaggggag 420
49 ctgggcaccg acctggttaag catcccccat ggccccaacg tcaactgtgcg tgccaacatt 480
50 gctgccatca ctgaatcaga caagtcttct atcaacggct ccaactggga aggcattcctg 540
51 gggctggcct atgctgagat tgccaggcct gacgactccc tggagccttt ctttgactct 600
52 ctggtaaagc agaccacagt tcccaacctc ttctccctgc agctttgtgg tgctggcttc 660
53 cccctcaacc agtctgaagt gctggcctct gtcggaggga gcatgatcat tggaggatc 720
54 gaccactcgc tgtacacagg cagtctctgg tatacaccca tccggcgga gtggtattat 780
55 gaggtgatca ttgtgcgggt ggagatcaat ggacaggatc tgaaaatgga ctgcaaggag 840
```

## RAW SEQUENCE LISTING

DATE: 12/23/2002

PATENT APPLICATION: US/09/471,669A

TIME: 12:15:54

Input Set : A:\Sub15270-006430US.app

Output Set: N:\CRF4\12232002\I471669A.raw

```

56 tacaactatg acaagagcat tgtggacagt ggcaccacca accttcgttt gcccaagaaa 900
57 gtgtttgaag ctgcagtcaa atccatcaag gcagcctcct ccacggagaa gttccctgat 960
58 ggtttctggc taggagagca gctggtgtgc tggcaagcag gcaccacccc ttggaacatt 1020
59 ttcccagtca tctcactcta cctaattgggt gaggttacca accagtcctt ccgcatcacc 1080
60 atccttccgc agcaataacct gcggccagtg gaagatgtgg ccacgtccca agacgactgt 1140
61 tacaagtttg ccatctcaca gtcatccacg ggcactgtta tgggagctgt tatcatggag 1200
62 ggcttctacg ttgtctttga tcgggcccga aaacgaattg gctttgctgt cagcgcttgc 1260
63 catgtgcacg atgagttcag gacggcagcg gtggaaggcc cttttgtcac cttggacatg 1320
64 gaagactgtg gctacaacat tccacagaca gatgagtcaa ccctcatgac catagcctat 1380
65 gtcatggctg ccatctgcgc cctcttcattg ctgccactct gcctcatggg gtgtcagtgg 1440
66 cgctgcctcc gctgcctgcg ccagcagcat gatgactttg ctgatgacat ctccctgctg 1500
67 aag 1503
70 <210> SEQ ID NO: 2
71 <211> LENGTH: 501
72 <212> TYPE: PRT
73 <213> ORGANISM: Homo sapiens
75 <400> SEQUENCE: 2
76 Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val
77 1 5 10 15
79 Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
80 20 25 30
82 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
83 35 40 45
85 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
86 50 55 60
88 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
89 65 70 75 80
91 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
92 85 90 95
94 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
95 100 105 110
97 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
98 115 120 125
100 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
101 130 135 140
103 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
104 145 150 155 160
106 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
107 165 170 175
109 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp
110 180 185 190
112 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
113 195 200 205
115 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
116 210 215 220
118 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
119 225 230 235 240
121 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
122 245 250 255

```

## RAW SEQUENCE LISTING

DATE: 12/23/2002

PATENT APPLICATION: US/09/471,669A

TIME: 12:15:54

Input Set : A:\Sub15270-006430US.app

Output Set: N:\CRF4\12232002\I471669A.raw

```

124 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
125           260           265           270
127 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
128           275           280           285
130 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
131           290           295           300
133 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
134 305           310           315           320
136 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
137           325           330           335
139 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
140           340           345           350
142 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
143           355           360           365
145 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
146           370           375           380
148 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
149 385           390           395           400
151 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
152           405           410           415
154 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
155           420           425           430
157 Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
158           435           440           445
160 Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala
161           450           455           460
163 Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp
164 465           470           475           480
166 Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp
167           485           490           495
169 Ile Ser Leu Leu Lys
170           500

```

173 &lt;210&gt; SEQ ID NO: 3

174 &lt;211&gt; LENGTH: 24

175 &lt;212&gt; TYPE: DNA

176 &lt;213&gt; ORGANISM: Homo sapiens

178 &lt;400&gt; SEQUENCE: 3

179 gagagacgar garccwgagg agcc

24

182 &lt;210&gt; SEQ ID NO: 4

183 &lt;211&gt; LENGTH: 24

184 &lt;212&gt; TYPE: DNA

185 &lt;213&gt; ORGANISM: Artificial Sequence

187 &lt;220&gt; FEATURE:

188 &lt;223&gt; OTHER INFORMATION: Description of Artificial Sequence: Degenerate

189 oligonucleotide primer derived from SEQ ID NO:2

191 &lt;400&gt; SEQUENCE: 4

192 gagagacgar garccwgaag agcc

24

195 &lt;210&gt; SEQ ID NO: 5

196 &lt;211&gt; LENGTH: 24

## RAW SEQUENCE LISTING

DATE: 12/23/2002

PATENT APPLICATION: US/09/471,669A

TIME: 12:15:54

Input Set : A:\Sub15270-006430US.app

Output Set: N:\CRF4\12232002\I471669A.raw

```

197 <212> TYPE: DNA
198 <213> ORGANISM: Artificial Sequence
200 <220> FEATURE:
201 <223> OTHER INFORMATION: Description of Artificial Sequence: Degenerate
202     oligonucleotide primer derived from SEQ ID NO:2
204 <400> SEQUENCE: 5
205 gagagacgar garccwgaag aacc                                     24
208 <210> SEQ ID NO: 6
209 <211> LENGTH: 24
210 <212> TYPE: DNA
211 <213> ORGANISM: Artificial Sequence
213 <220> FEATURE:
214 <223> OTHER INFORMATION: Description of Artificial Sequence: Degenerate
215     oligonucleotide primer derived from SEQ ID NO:2
217 <400> SEQUENCE: 6
218 gagagacgar garccwgagg aacc                                     24
221 <210> SEQ ID NO: 7
222 <211> LENGTH: 23
223 <212> TYPE: DNA
224 <213> ORGANISM: Artificial Sequence
226 <220> FEATURE:
227 <223> OTHER INFORMATION: Description of Artificial Sequence: Degenerate
228     oligonucleotide primer derived from SEQ ID NO:2
230 <400> SEQUENCE: 7
231 agagacgarg arccsgagga gcc                                     23
234 <210> SEQ ID NO: 8
235 <211> LENGTH: 23
236 <212> TYPE: DNA
237 <213> ORGANISM: Artificial Sequence
239 <220> FEATURE:
240 <223> OTHER INFORMATION: Description of Artificial Sequence: Degenerate
241     oligonucleotide primer derived from SEQ ID NO:2
243 <400> SEQUENCE: 8
244 agagacgarg arccsgaaga gcc                                     23
247 <210> SEQ ID NO: 9
248 <211> LENGTH: 23
249 <212> TYPE: DNA
250 <213> ORGANISM: Artificial Sequence
252 <220> FEATURE:
253 <223> OTHER INFORMATION: Description of Artificial Sequence: Degenerate
254     oligonucleotide primer derived from SEQ ID NO:2
256 <400> SEQUENCE: 9
257 agagacgarg arccsgaaga acc                                     23
260 <210> SEQ ID NO: 10
261 <211> LENGTH: 23
262 <212> TYPE: DNA
263 <213> ORGANISM: Artificial Sequence
265 <220> FEATURE:
266 <223> OTHER INFORMATION: Description of Artificial Sequence: Degenerate

```

## RAW SEQUENCE LISTING

DATE: 12/23/2002

PATENT APPLICATION: US/09/471,669A

TIME: 12:15:54

Input Set : A:\Sub15270-006430US.app

Output Set: N:\CRF4\12232002\I471669A.raw

```

267     oligonucleotide primer derived from SEQ ID NO:2
269 <400> SEQUENCE: 10
270 agagacgarg arccsgagga acc                                23
273 <210> SEQ ID NO: 11
274 <211> LENGTH: 23
275 <212> TYPE: DNA
276 <213> ORGANISM: Artificial Sequence
278 <220> FEATURE:
279 <223> OTHER INFORMATION: Description of Artificial Sequence: Degenerate
280     oligonucleotide primer derived from SEQ ID NO:2
282 <400> SEQUENCE: 11
283 cgtcacagrt trtcaaccat ctc                                23
286 <210> SEQ ID NO: 12
287 <211> LENGTH: 23
288 <212> TYPE: DNA
289 <213> ORGANISM: Artificial Sequence
291 <220> FEATURE:
292 <223> OTHER INFORMATION: Description of Artificial Sequence: Degenerate
293     oligonucleotide primer derived from SEQ ID NO:2
295 <400> SEQUENCE: 12
296 cgtcacagrt trtctaccat ctc                                23
299 <210> SEQ ID NO: 13
300 <211> LENGTH: 23
301 <212> TYPE: DNA
302 <213> ORGANISM: Artificial Sequence
304 <220> FEATURE:
305 <223> OTHER INFORMATION: Description of Artificial Sequence: Degenerate
306     oligonucleotide primer derived from SEQ ID NO:2
308 <400> SEQUENCE: 13
309 cgtcacagrt trtccaccat ctc                                23
312 <210> SEQ ID NO: 14
313 <211> LENGTH: 23
314 <212> TYPE: DNA
315 <213> ORGANISM: Artificial Sequence
317 <220> FEATURE:
318 <223> OTHER INFORMATION: Description of Artificial Sequence: Degenerate
319     oligonucleotide primer derived from SEQ ID NO:2
321 <400> SEQUENCE: 14
322 cgtcacagrt trtcgaccat ctc                                23
325 <210> SEQ ID NO: 15
326 <211> LENGTH: 23
327 <212> TYPE: DNA
328 <213> ORGANISM: Artificial Sequence
330 <220> FEATURE:
331 <223> OTHER INFORMATION: Description of Artificial Sequence: Degenerate
332     oligonucleotide primer derived from SEQ ID NO:2
334 <400> SEQUENCE: 15
335 cgtcacagrt trtcaaccat ttc                                23
338 <210> SEQ ID NO: 16

```

RAW SEQUENCE LISTING ERROR SUMMARY  
PATENT APPLICATION: US/09/471,669A

DATE: 12/23/2002  
TIME: 12:15:55

Input Set : A:\Sub15270-006430US.app  
Output Set: N:\CRF4\12232002\I471669A.raw

Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:22; N Pos. 12  
Seq#:23; N Pos. 12  
Seq#:24; N Pos. 12  
Seq#:25; N Pos. 12  
Seq#:26; N Pos. 7  
Seq#:27; N Pos. 7  
Seq#:28; N Pos. 3,12  
Seq#:29; N Pos. 3,12  
Seq#:34; N Pos. 16  
Seq#:35; N Pos. 16  
Seq#:36; N Pos. 16  
Seq#:37; N Pos. 16  
Seq#:48; N Pos. 6164,6238,6254,6255,6256,6257,6258,6259,6260,6261,6262,6263  
Seq#:48; N Pos. 6264,6265,6266,6267,6268,6269,6270,6271,6272  
Seq#:61; Xaa Pos. 4  
Seq#:72; Xaa Pos. 10  
Seq#:73; Xaa Pos. 5  
Seq#:76; N Pos. 6,18,27,30,33,36,39,42,48,57  
Seq#:78; Xaa Pos. 3  
Seq#:81; Xaa Pos. 4

Invalid Line Length:

The rules require that a line not exceed 72 characters in length. This includes spaces.

Seq#:1; Line(s) 1

## VERIFICATION SUMMARY

DATE: 12/23/2002

PATENT APPLICATION: US/09/471,669A

TIME: 12:15:55

Input Set : A:\Sub15270-006430US.app

Output Set: N:\CRF4\12232002\I471669A.raw

L:431 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:22 after pos.:0  
L:449 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:23 after pos.:0  
L:467 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:24 after pos.:0  
L:485 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:25 after pos.:0  
L:503 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:26 after pos.:0  
L:521 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:27 after pos.:0  
L:539 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:28 after pos.:0  
L:557 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:29 after pos.:0  
L:627 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:34 after pos.:0  
L:645 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:35 after pos.:0  
L:663 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:36 after pos.:0  
L:681 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:37 after pos.:0  
L:1082 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:48 after pos.:6120  
L:1083 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:48 after pos.:6180  
L:1084 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:48 after pos.:6240  
L:1713 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:61 after pos.:0  
L:2396 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:72 after pos.:0  
L:2415 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:73 after pos.:0  
L:2594 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:76 after pos.:0  
L:2626 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:78 after pos.:0  
L:2674 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:81 after pos.:0